UPMC LIFE CHANGING MEDICINE


# Health and Safety Consequences of Psychostimulant Use

Michael Lynch, MD
Medical Director, Pittsburgh Poison Center
Assistant Professor of Emergency Medicine, Toxicology, and Pediatrics
University of Pittsburgh

# Objectives

- Discuss the root causes and neurobiology of substance use
- Understand the pharmacology and effects of stimulants and hallucinogens
- Describe the presentation and treatment of stimulant and hallucinogen toxicity
- Review trends in the use, misuse, and overdose on stimulants, hallucinogens, and synthetics analogues

# Neurobiology of Addiction

- Genetic
  - Increased risk in first degree relatives of individuals with any substance use disorder
- Psychosocial
  - Increased environmental availability and decreased perceived threat
  - Physical and/or psychological trauma
  - Impaired coping mechanisms
- Pharmacologic
  - Dopamine-mediated reward
  - Tolerance
  - Long term changes in stress response pathways



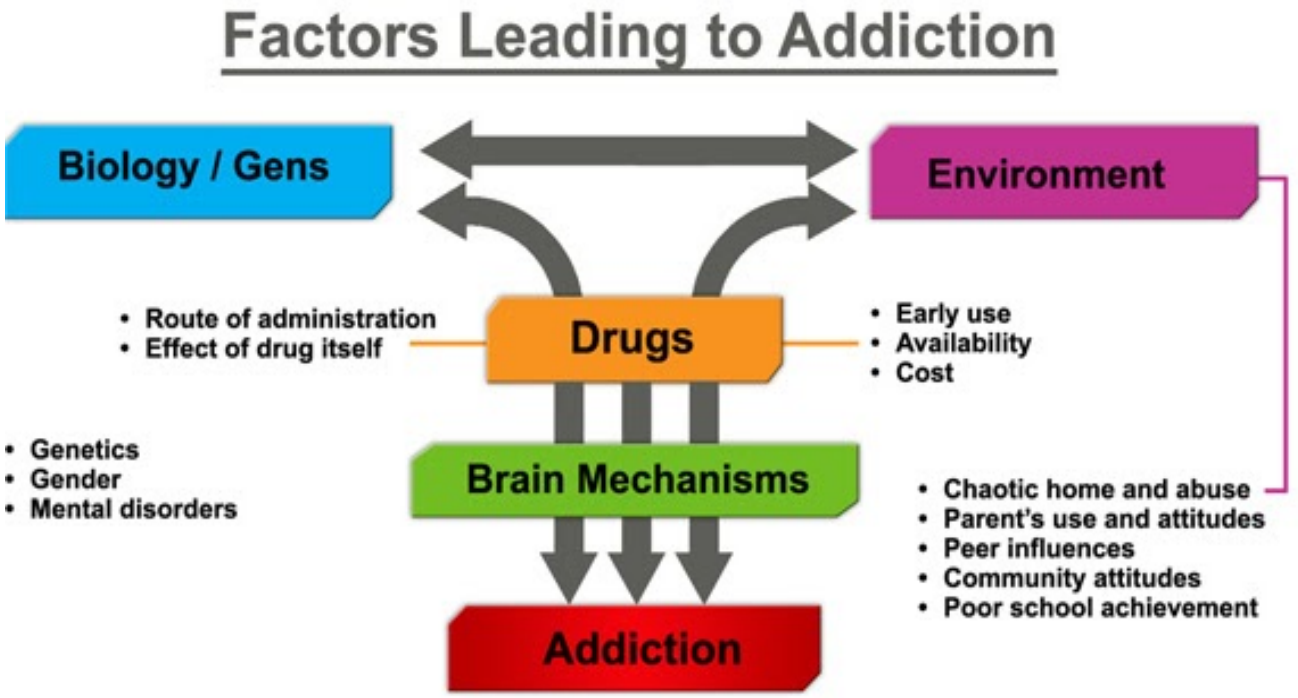
Bart G. Maintenance Medication for Opiate Addiction: The Foundation of Recovery. *J Addict Dis.* 2012 July; 31(3): 207-225.

# Development of Addiction

- Nature vs. Nurture?

YES!

  - 23-54% due to genetics in multiple studies[1,2]
  - 25% attributable to family environmental factors
  - 44% attributable to non-family environmental factors






1. Tsuang MT, Lyons MJ, Meyer JM , et al. Co-occurrence of abuse of different drugs in men: The role of drug-specific and shared vulnerabilities. Arch Gen Psychiatry. 1998;55(11):967–72
2. Crist RC, Reiner BC, Berrettini WH. A review of opioid addiction genetics. Curr Opin Psychol. 2018 Aug 9; 27-31.

# Environmental Risk Factors for Addiction Development

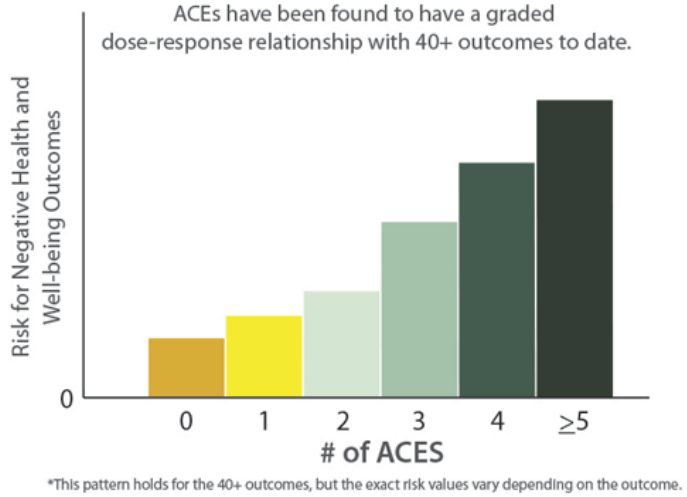
- Adolescent exposure to drugs or heavy drinking
- Low socioeconomic status
- Lack of social support systems
- Parental drug or alcohol use
- Parental depression
- Peer/sibling influences
- Drug availability
- School and neighborhood characteristics
- Trauma (ACES)

## ACES can have lasting effects on….

Health (obesity, diabetes, depression, suicide attempts, STDs, heart disease, cancer, stroke, COPD, broken bones)

Behaviors (smoking, alcoholism, drug use)

Life Potential (graduation rates, academic achievement, lost time from work)

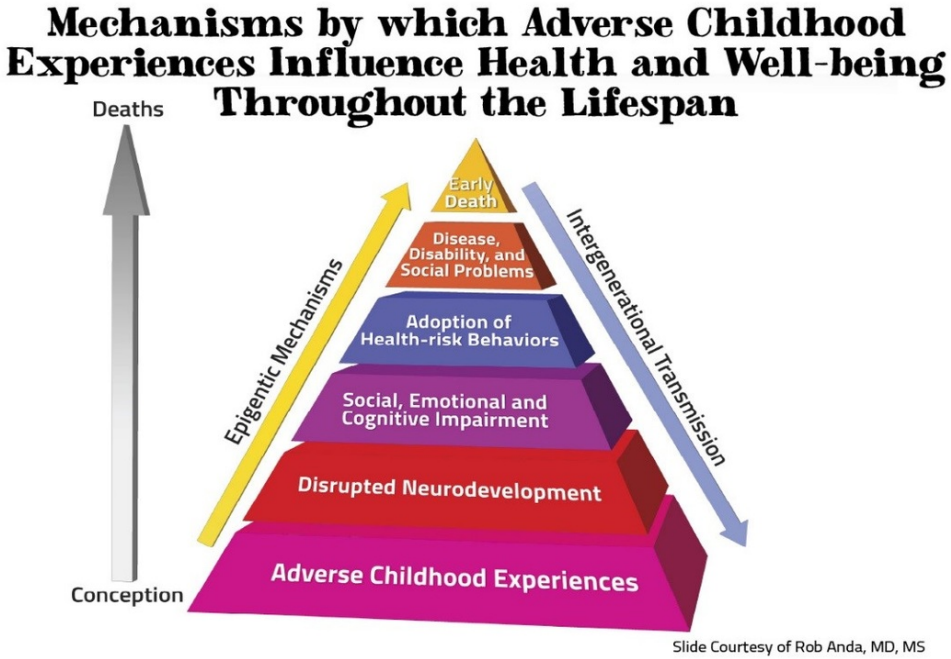




1. Hawkins JD, Catalano RF, Miller JY. Risk and protective factors for alcohol and other drug problems in adolescence and early adulthood: implications for substance abuse prevention. Psychol Bull 1992; 112: 64–105
2. Sloboda Z, Glantz MD, Tarter RE. Revisiting the concepts of risk and protective factors for understanding the etiology and development of substance use and substance use disorders: implications for prevention. Subst Use Misuse 2012; 47: 944–62
3. CDC. https://www.cdc.gov/violenceprevention/childabuseandneglect/acestudy/ace-graphics.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fviolenceprevention%2Facestudy%2FACE_graphics.html

# ACES Through the Generations

- ~8 million children live with an adult who has a substance use disorder[1]
- Parents with SUD are 3x more likely to physically or sexually abuse their children
- From 1999-2014, incidence of parental substance use as a reason for child removal **doubled** (15.8→31.8%)[2]
- From 2004-2013, incidence of neonatal abstinence syndrome more than **tripled** (7 cases/1,000 admissions → 27 cases/1,000 admissions)[3]

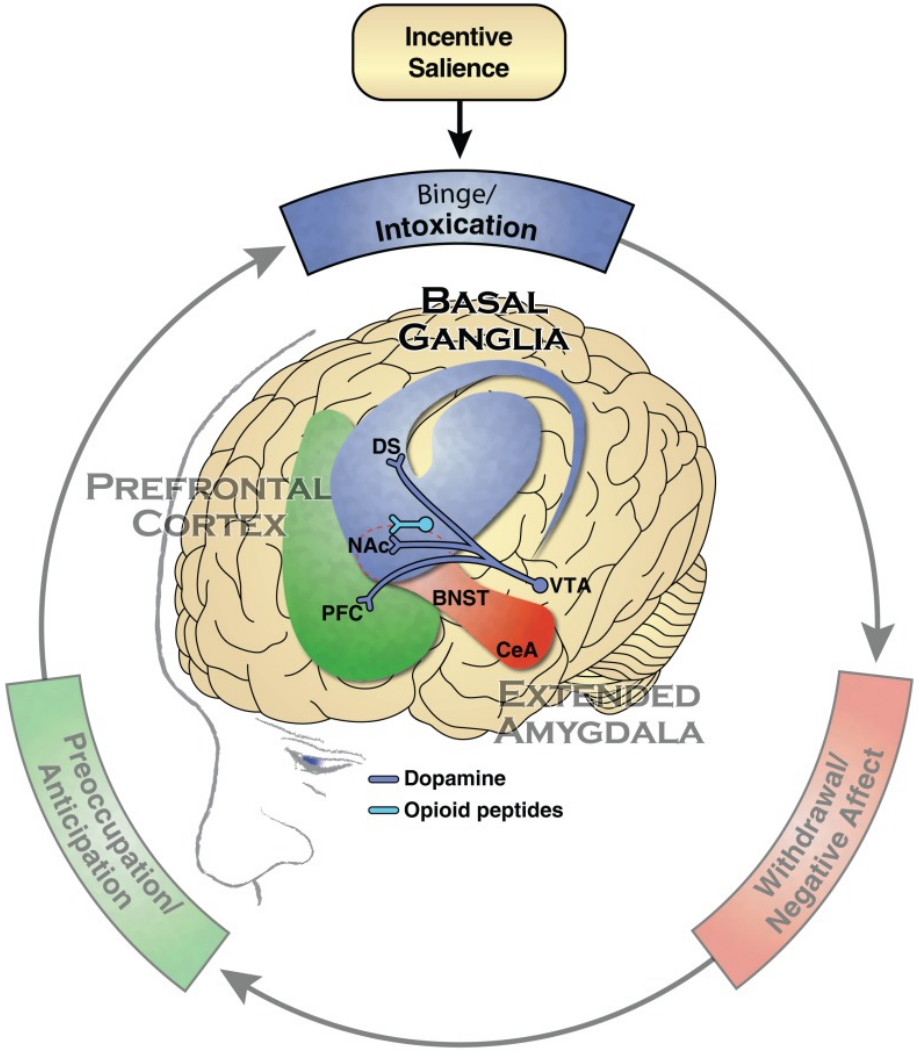




1. Lander L, Howsare J, Byrne M. The impact of substance use disorders on families and children: From theory to practice. Social Work in Public Health 28 (2013): 194-205
2. http://www.ncsl.org/research/human-services/substance-abuse-and-child-welfare-resources.aspx
3. Tolia VN, Patrick SW, Bennett MM, Murthy K, Sousa J, Smith PB, Clark RH, Spitzer AR. Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. N Engl J Med. 2015 May 28; 372(22): 2118-26

# Neuropharmacology of Drug Addiction

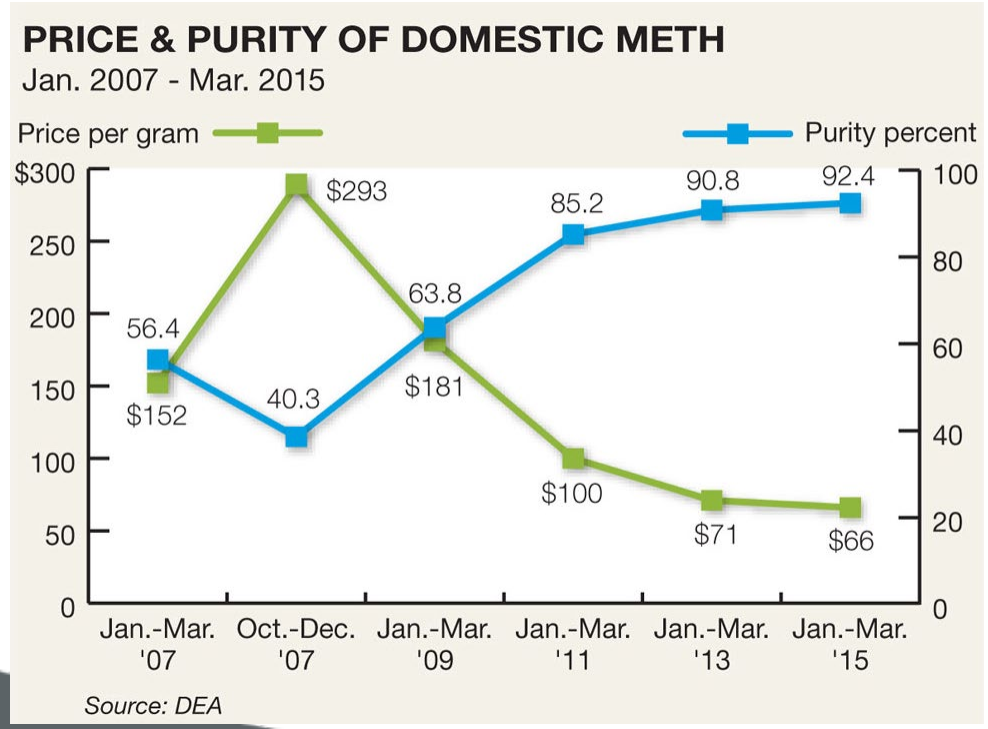
- Neurotransmitters Involved
  - Dopamine
  - Opioid
  - GABA
  - Glutamate
  - Serotonin
  - Acetylcholine
  - Endocannabinoids
  - Enkephalins
  - Norepinephrine
  - Corticotropin-releasing factor
  - Dynorphin
  - Neuropeptide Y

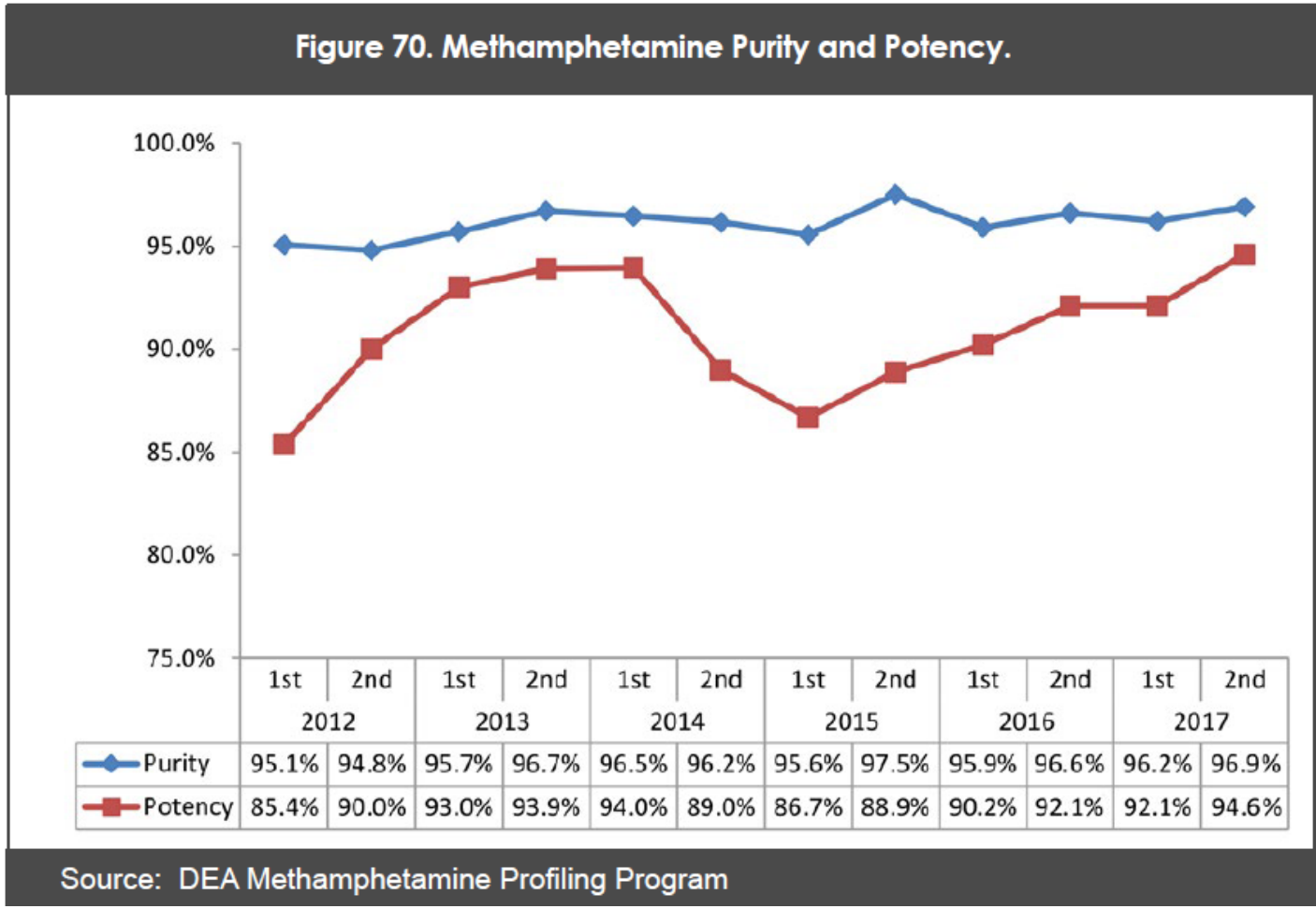


# Stimulant Purity and Availability

- Cocaine and methamphetamine purity and availability have increased

- Price per gram has also decreased



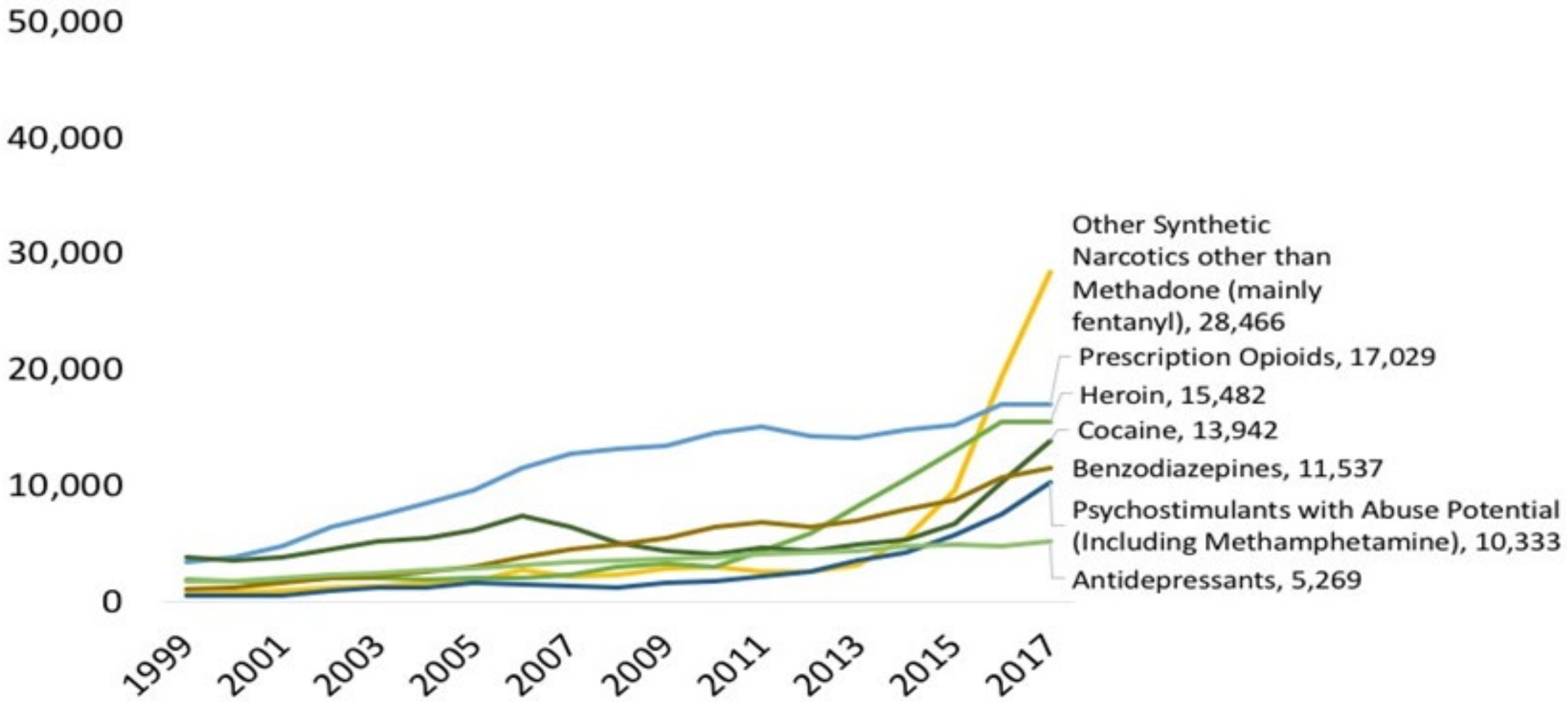




| | 1st 2012 | 2nd 2012 | 1st 2013 | 2nd 2013 | 1st 2014 | 2nd 2014 | 1st 2015 | 2nd 2015 | 1st 2016 | 2nd 2016 | 1st 2017 | 2nd 2017 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Purity | 95.1% | 94.8% | 95.7% | 96.7% | 96.5% | 96.2% | 95.6% | 97.5% | 95.9% | 96.6% | 96.2% | 96.9% |
| Potency | 85.4% | 90.0% | 93.0% | 93.9% | 94.0% | 89.0% | 86.7% | 88.9% | 90.2% | 92.1% | 92.1% | 94.6% |



U.S. Department of Justice, Drug Enforcement Administration. 2018 National Drug Threat Assessment. Accessed at: https://www.dea.gov/sites/default/files/2018-11/DIR-032-18%202018%20NDTA%20final%20low%20resolution.pdf on 7/15/2019.

# Substances Associated with Overdose Deaths

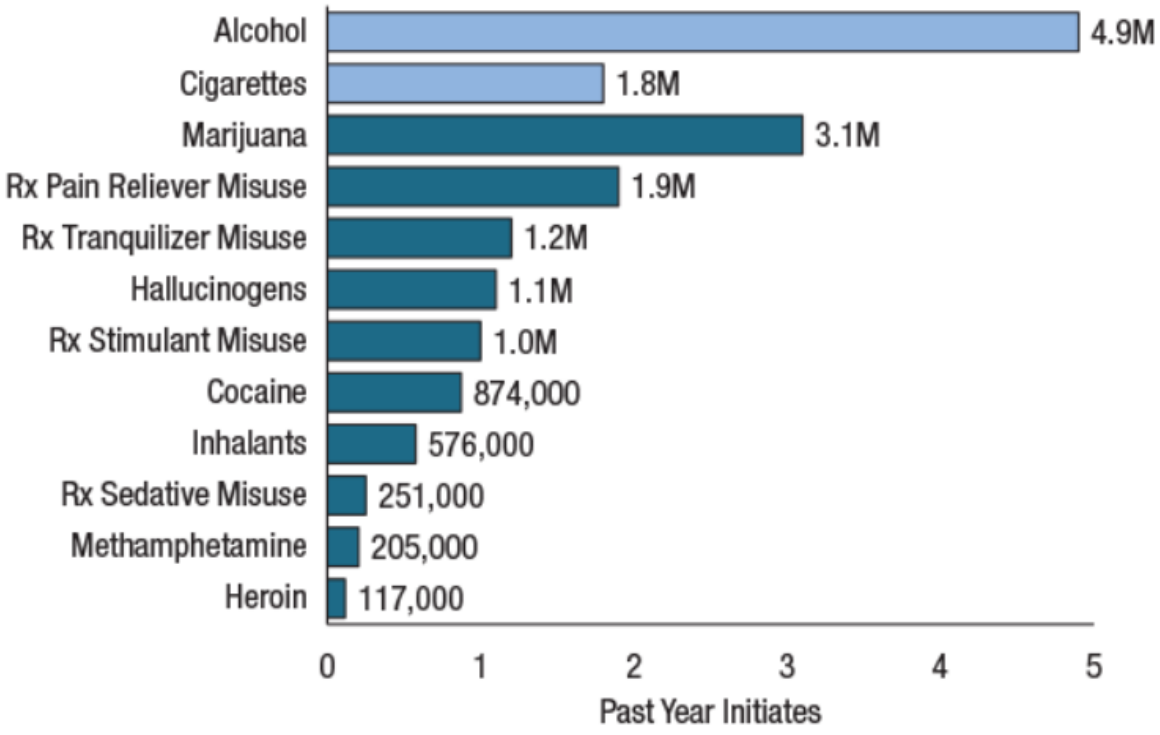



Source: : Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018

# Stimulant Misuse

- New stimulant misuse surpasses new opioid misuse
- 2,079,000 vs. 2,017,000

**Figure 26. Past Year Initiates of Substances among People Aged 12 or Older: 2018**



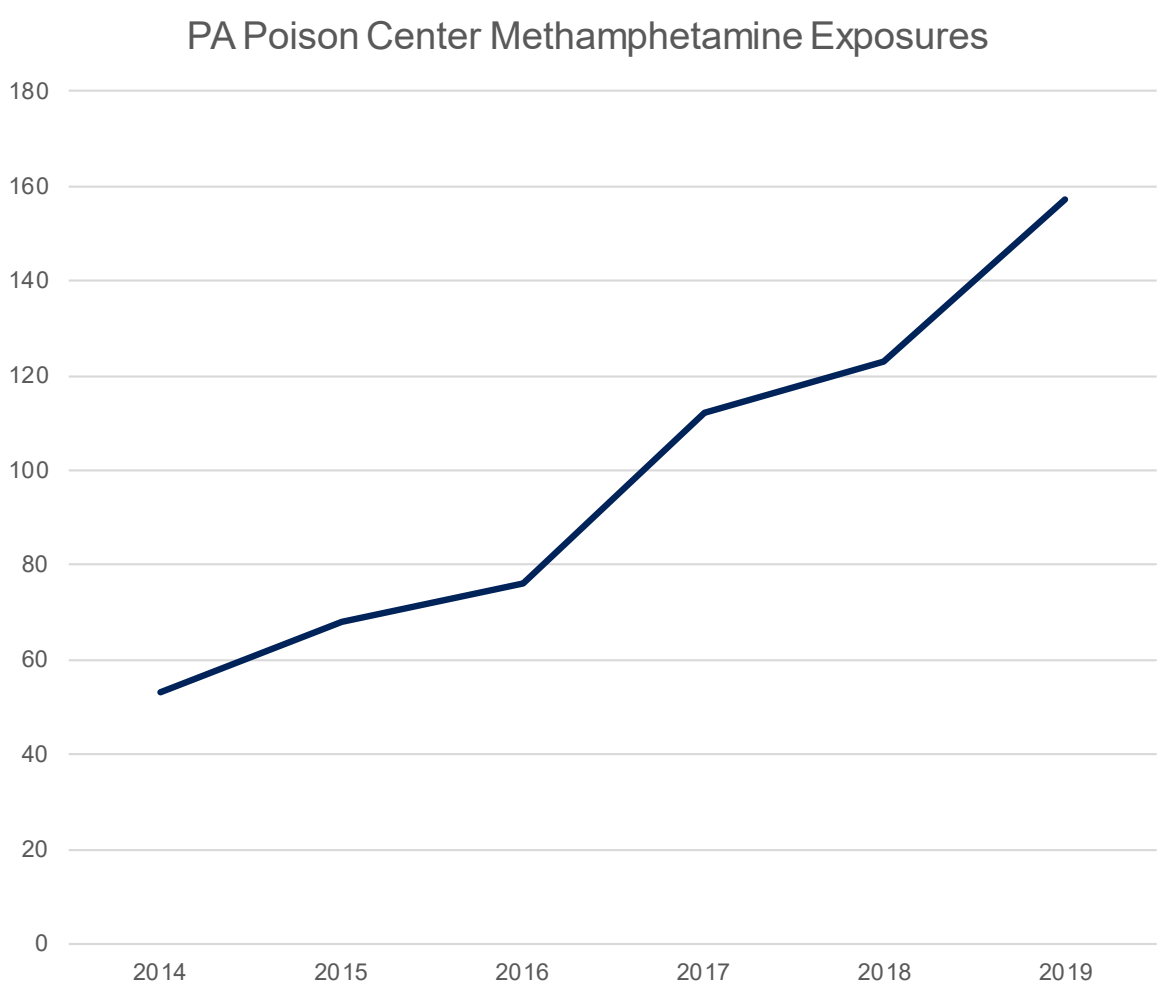

Rx = prescription.

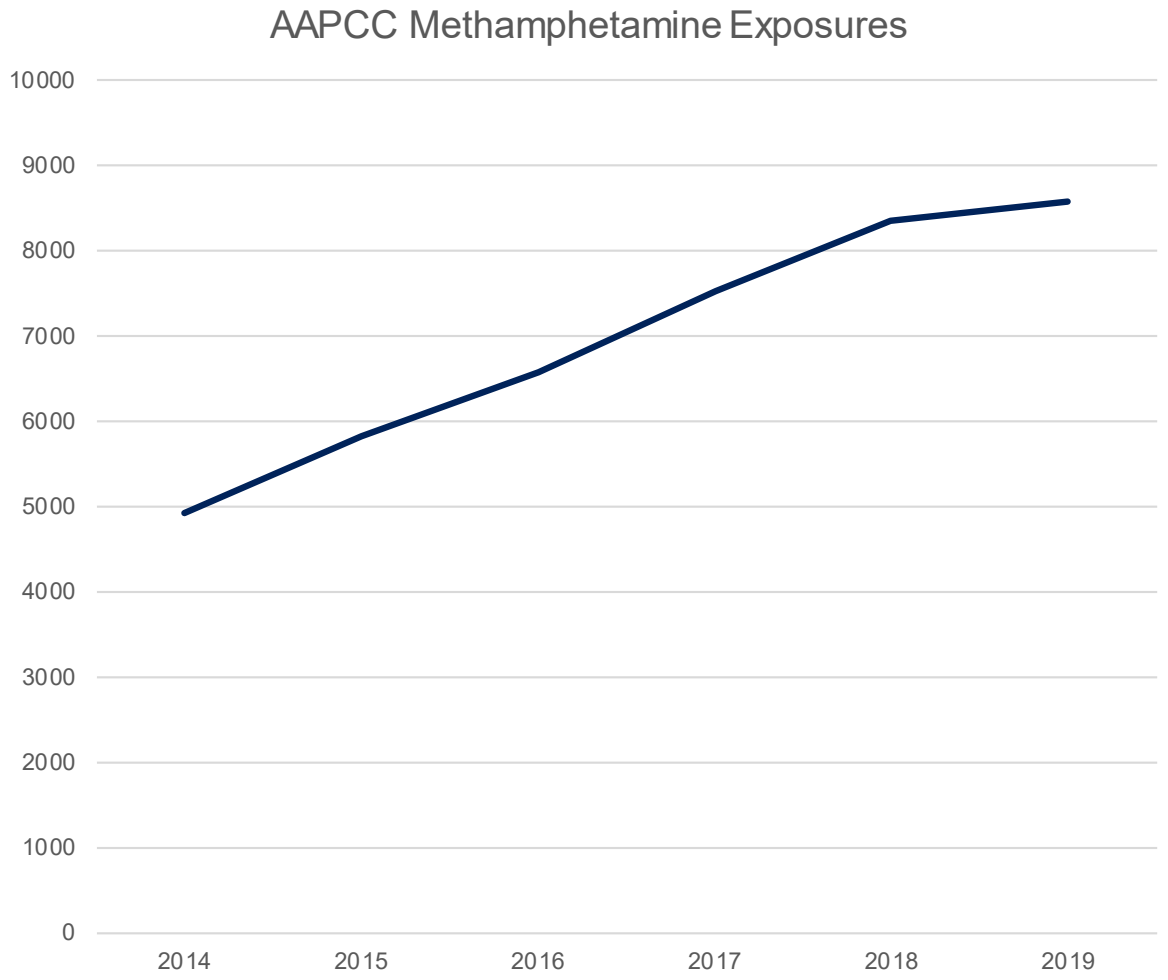
Note: Estimates for prescription pain relievers, prescription tranquilizers, prescription stimulants, and prescription sedatives are for the initiation of misuse.



Substance Abuse and Mental Health Services Administration. (2019). *Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health* (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/

# Methamphetamine Exposures Reported to Poison Centers-PA and U.S.

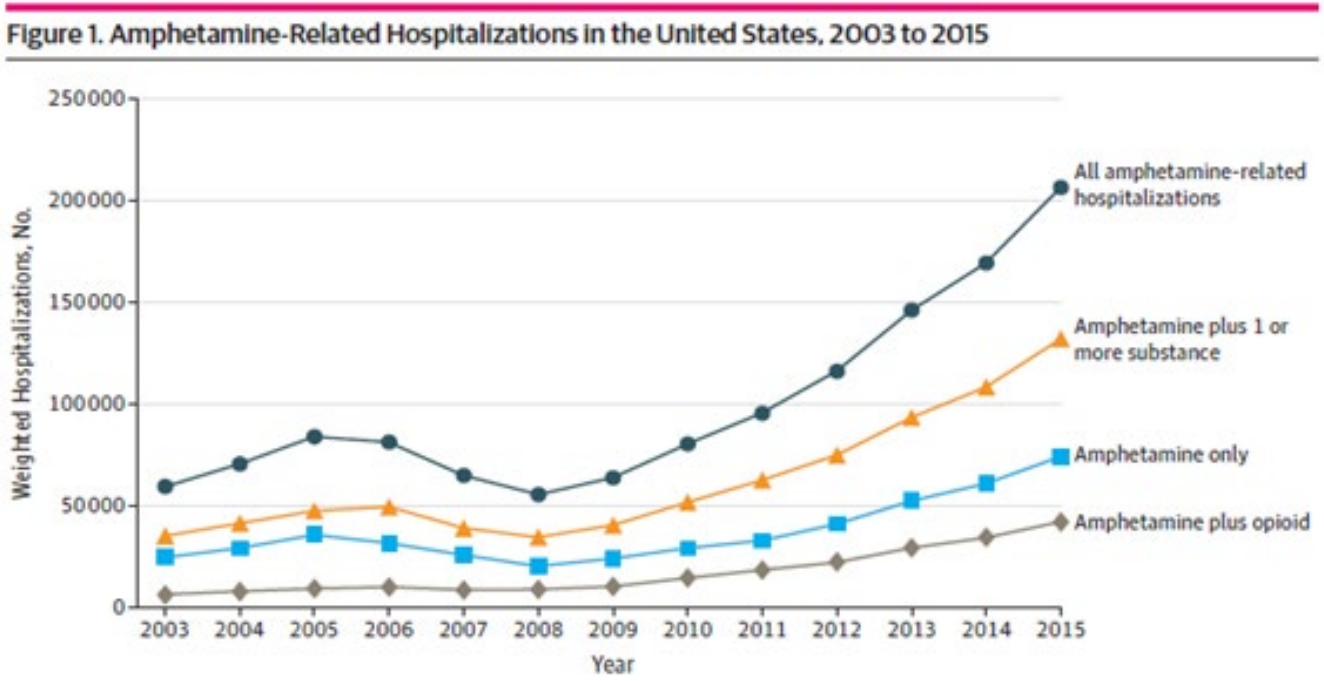


# Hospital Costs Associated with Stimulants

- Amphetamine-related hospital costs increased almost 400% from 2003 to 2015[1]
  - 2003: ~$436 million
  - 2015: ~$2.17 billion

- Pennsylvania[2]:
  - Cocaine related hospitalizations **+27%** from 2016 to 2019
  - Amphetamine related hospitalizations **+66%** from 2016 to 2019





1. Winkelman TNA, Admon LK, Jennings L, Shippee ND, Richardson CR, Bart G. Evaluation of Amphetamine-Related Hospitalizations and Associated Clinical Outcomes and Costs in the United States. *JAMA Netw Open.* Published online October 19, 20181(6):e183758
2. Hospitalizations for Opioid Overdose: Three-Year Review. PA Health Care Cost Containment Council. September 2019.

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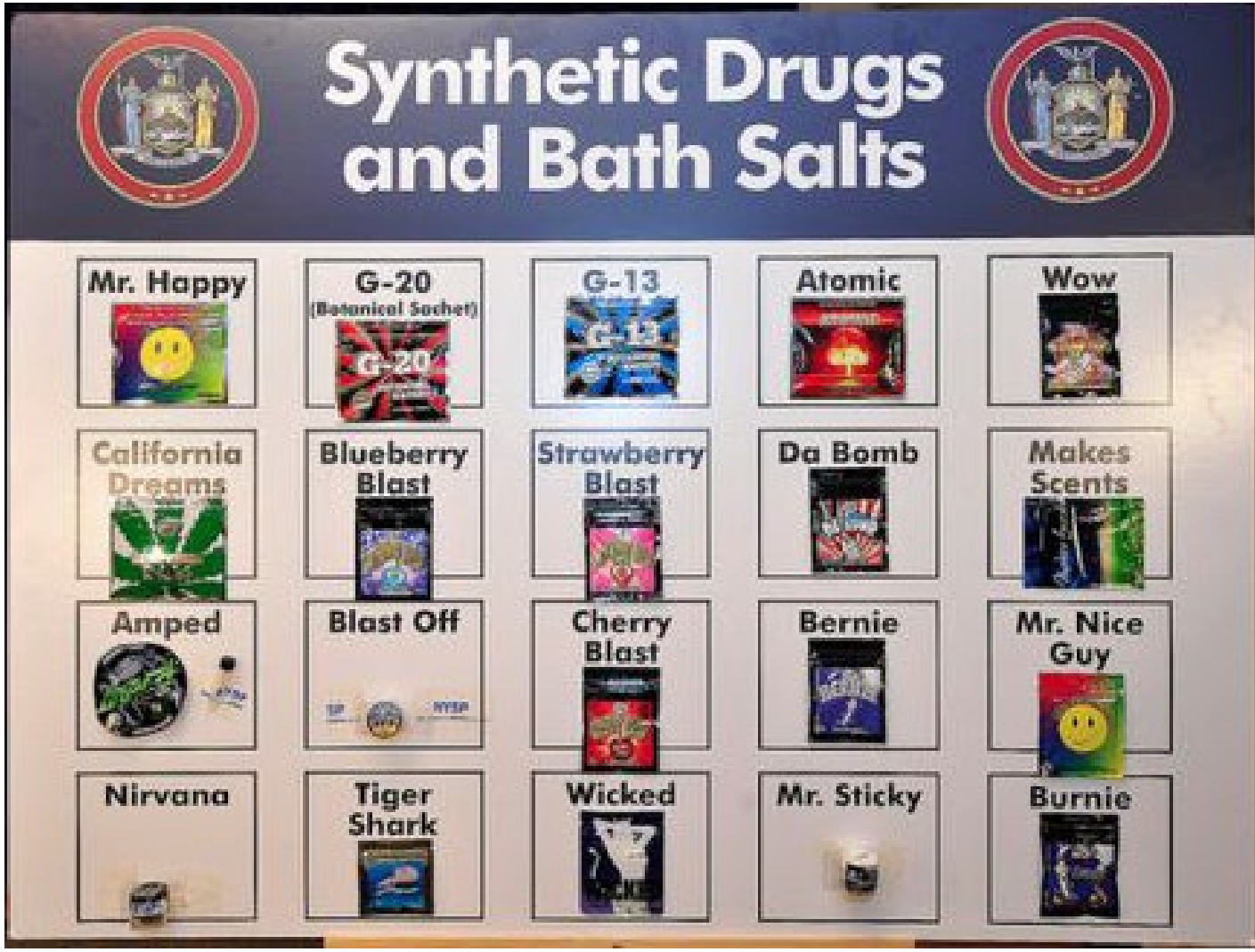
# Stimulants and Hallucinogens-Examples

- Cocaine
- Amphetamines, Rx and illicit
- Methamphetamine
- Cathinones (“bath salts”)
- Synthetic hallucinogenic stimulants
  - 25i-NBOMe (“N-bombs”, “acid”)
  - 2C, 2C-I
- Dissociative Agents
  - Phencyclidine, methoxetamine
- Serotonergic hallucinogens
  - Dimethyltryptamine (DMT)
  - MDMA (“Molly”)

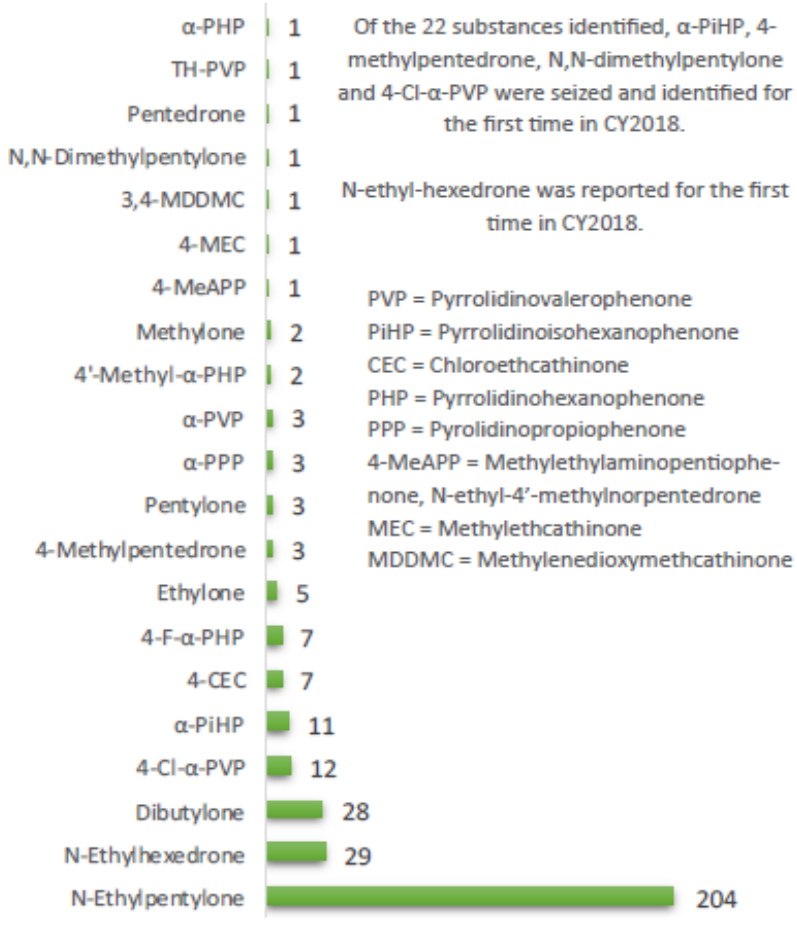


# Variety is the Spice of Life

- Synthetic Stimulants and Hallucinogens seized by DEA in 2018
  - 2C-B
  - 25i-NBOMe
  - 25B-NBOMe
  - 25C-NBOMe
  - 2C-H
  - 2C-I
  - 3-MeO-PCP
  - 2F-Deschloroketamine
  - 2-Oxo-PCE
  - MMMP
  - 4-Fluoroamphetamine
  - 5-MeO-DALT
  - 5-MeO-DiPT

## CATHINONES

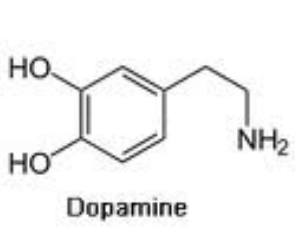
THERE WERE 327 CATHINONE IDENTIFICATIONS THIS REPORTING PERIOD. N-ETHYLPENTYLONE CONTINUES TO BE THE MOST REPORTED CATHINONE, ACCOUNTING FOR APPROXIMATELY 62% OF THE IDENTIFICATIONS.



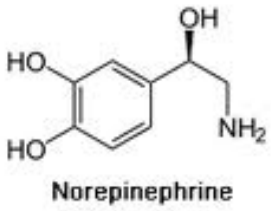

DEA. 2018 Annual Emerging Threat Report.

# Stimulant Pathophysiology

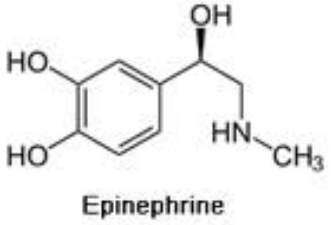
- Cocaine, amphetamine-based stimulants, and cathinones
- Direct receptor activation
- Inhibition of reuptake of biogenic amines
  - Serotonin
  - Norepinephrine
  - Dopamine
- Toxicity is related to relative effects on each transmitter/receptor system



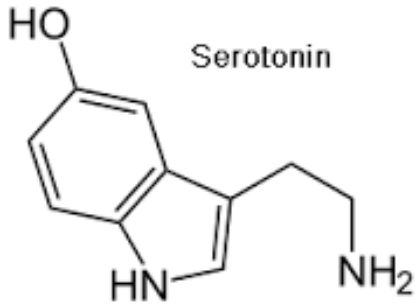
Dopamine

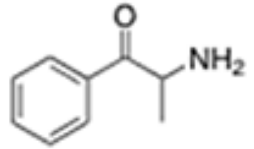


Norepinephrine

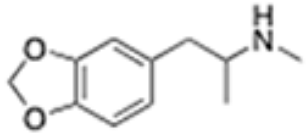


Epinephrine

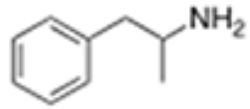


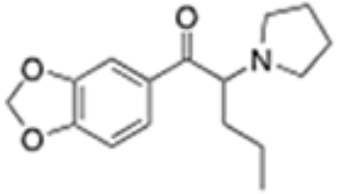
Cathinone



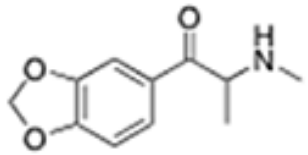
MDMA



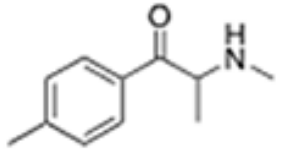
Amphetamine



MDPV



Methylone (bk-MDMA)



4-MMC

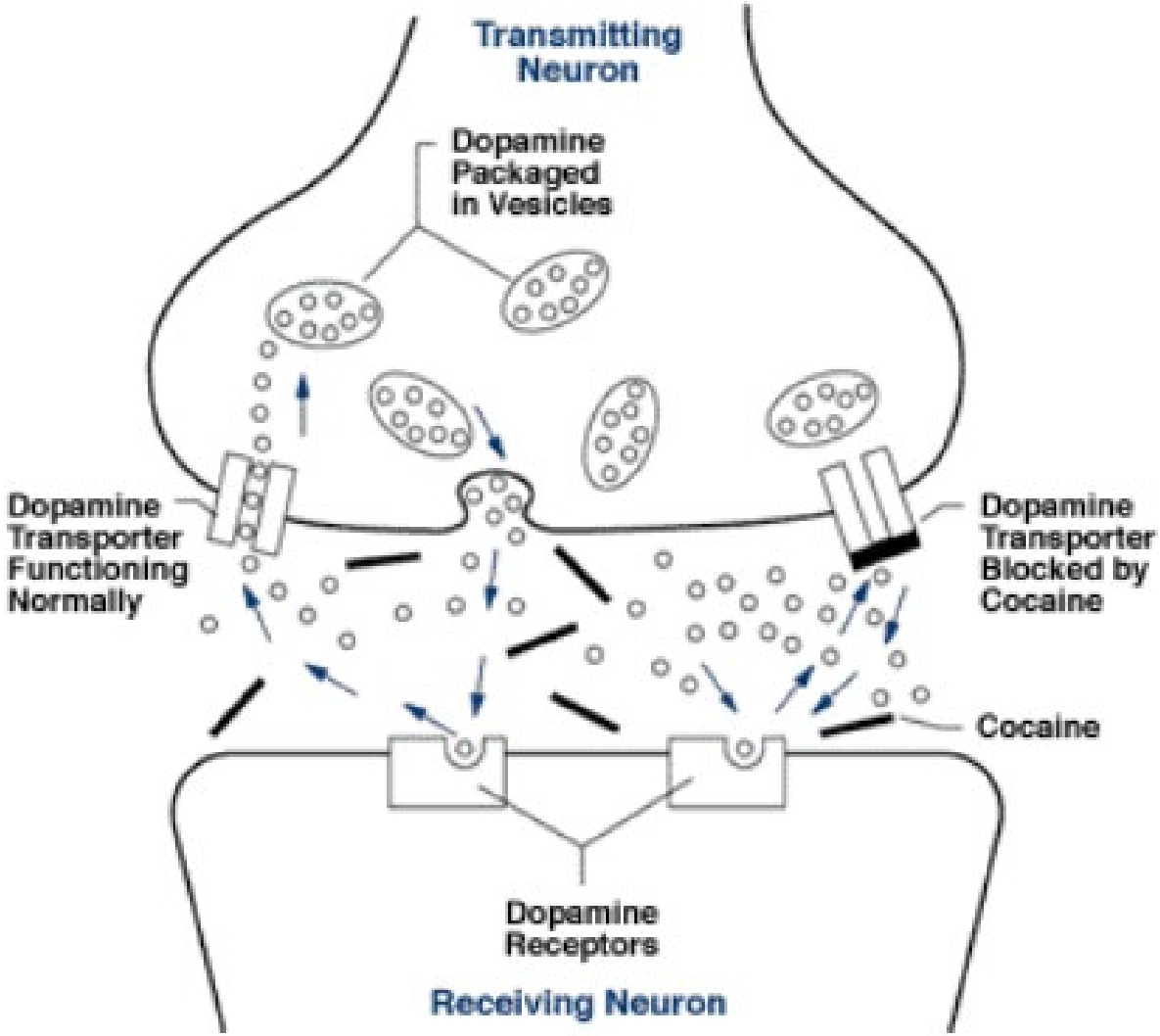
# Hallucinogenic Stimulant Pathophysiology- Serotonin

- Variety of serotonin receptor subtypes
- Activation results in euphoria
- Hallucinogenic effects
  - Primarily visual and tactile; synesthesias
- Serotonin syndrome
- SIADH with low sodium (particularly with MDMA)

# Stimulant Pathophysiology-Norepinephrine and Dopamine

- Norepinephrine
  - Tachydysrhythmias
  - Agitation
  - Delirium
  - Hypertension
  - Seizures
  - Mydriasis

- Dopamine
  - Tachydysrhythmias
  - Hallucinations (visual and tactile)
  - Choreathetosis




http://archivetemp.iqscloud.net/NIDA_Notes/NNVol13N2/Brain.html

# Dissociative Agents

- Ketamine, phencyclidine, dextromethorphan, methoxyphencyclidine, methoxetamine

- NMDA receptor antagonists
  - Dissociated high; out of body
  - Stupor or agitation
  - Analgesic properties
  - Horizontal and vertical nystagmus
  - Tachycardia and mild hypertension
  - Mydriasis

# Acute Stimulant Toxicity

- Vital signs:
  - Hypertension and tachycardia
  - **HYPERTHERMIA**
- Agitation, delirium
- Seizures
- Intracranial hemorrhage, myocardial infarction and dysrhythmia
- Rhabdomyolysis
- Metabolic and/or respiratory acidosis
- Mydriasis
- Diaphoresis

# Treatment of Hallucinogenic-Stimulant Toxicity

- Control agitation and/or seizures
  - Benzodiazepines
  - Antipsychotics
  - Ketamine
  - Propofol
  - **NO NALOXONE-LIKE ANTIDOTE**
- Airway management as needed
- Once adequately sedated, additional cardiovascular management
- Cooling and hydration

# Chronic Stimulant Health Effects

- Pulmonary hypertension
  - 10x increased risk in patients with stimulant use
- Vasculitis
  - Drug-induced
  - Levamisole adulteration
- Increased platelet aggregation
- Atherosclerotic artery disease
- Psychosis



1. Havakuk O, Rezkalla SH, Kloner RA. The Cardiovascular Effects of Cocaine. J Am Coll Cardiol. 2017 Jul 4; 70(1): 101-113.
2. Chamarthi G, Lee Loy J, Koratala A. Methamphetamine-induced renal pseudovasculitis: Suspicion is the key. Clin Case Rep. 2018 Dec 28; 7(2): 381-382.
3. Ho EL, Josephson SA, Lee HS, Smith WS. Cerebrovascular complications of methamphetamine abuse. Neurocrit Care. 2009; 10(3): 295-305.
4. Glasner-Edwards S, Mooney LJ. Methamphetamine psychosis: epidemiology and management. CNS Drugs. 2014 Dec; 28(12): 1115-26.

# Synthetic Cannabinoids

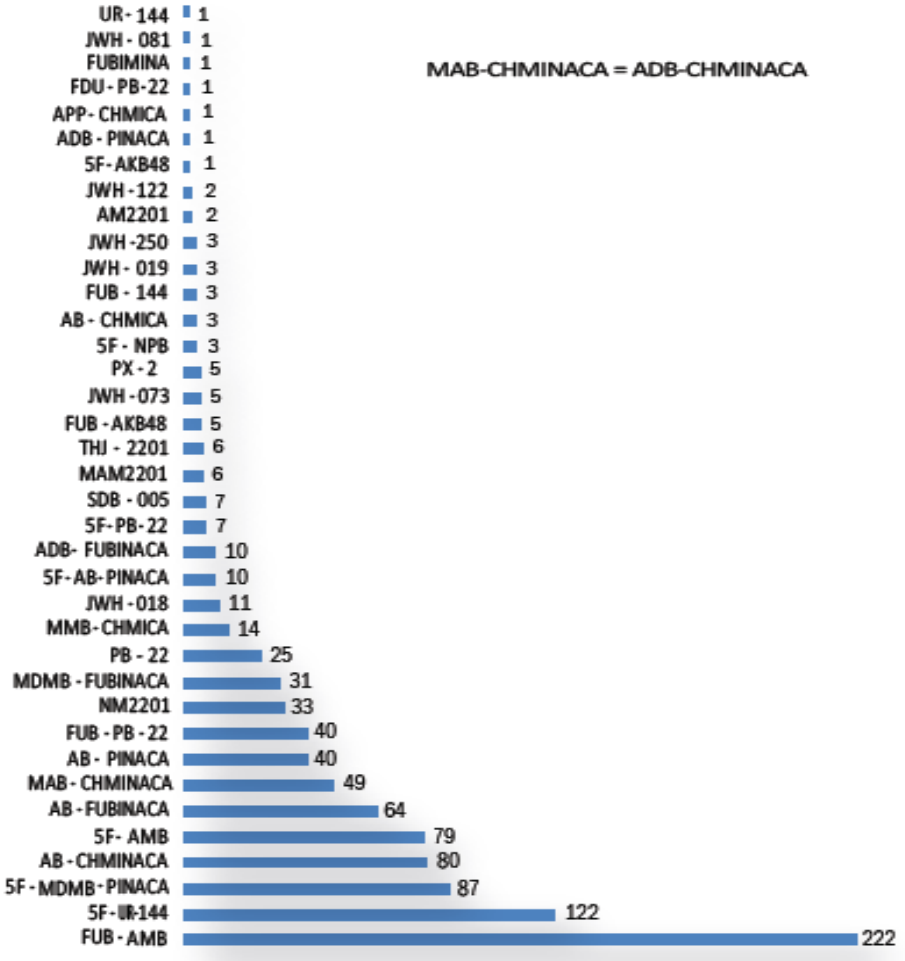
- Alkylindoles and cyclohexylphenols
- JWH, HU, and CP series Compounds
  - Sold as incense or potpourri in the U.S. since ~2010
  - Originally popularized in the U.K. and Europe in the mid-2000s
  - "Spice" and "K2" are common slang
- **Full cannabinoid agonists** leading to potent clinical effects

# "-INACA" Compounds

- Indazole carboxamides
- Marked increase in use reported in early 2015
- True prevalence difficult to assess given limited testing capabilities
- Chemicals sprayed onto dried vegetative material, e.g. tobacco or marijuana
- ADB-CHMINACA identified in PA overdose patients
  - Allentown area in 4/15/15 with 8 associated deaths
  - ~100 to UPMC Hamot in 10/15-12/15 with ~15% requiring intubation

# SYNTHETIC CANNABINOIDS

THERE WERE 984 SYNTHETIC CANNABINOID IDENTIFICATIONS IN CY 2016. FUB-AMB AND 5F-UR-144 WERE THE MOST COMMONLY REPORTED SYNTHETIC CANNABINOIDS, ACCOUNTING FOR APPROXIMATELY 34% OF THE SYNTHETIC CANNABINOID IDENTIFICATIONS DURING THE REPORTING PERIOD. Of the 37 different synthetic cannabinoids identified, three (~8%) of these substances, PX-2, MMB-CHMICA, and AB-CHMICA, were seized and reported for the first time in 2016.




MAB-CHMINACA = ADB-CHMINACA

# Synthetic Cannabinoid Clinical Effects

- Severe agitation/psychosis
- Delirium
- Sinus tachycardia and hypertension
- Rhabdomyolysis
- Respiratory failure

- Initial agitation often followed by deep sedation

# Chronic Cannabinoid Health Effects

- Largely unknown for newer synthetic cannabinoids
- Chronic adverse health effects associated with cannabinoid use
  - Addiction (9% of users; 17% in adolescents)
  - Lower IQ and increased dropout rates in adolescents
  - Diminished life satisfaction and achievement
  - Chronic bronchitis
  - Increased risk of psychosis

Volkow ND et al. Adverse Health Effects of Marijuana Use. *N Engl J Med*. 2014; 370: 2219-27.

# Just a Click Away…

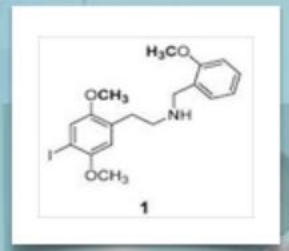
- Bath Salts Page 1
- Bath Salts Page2
- Bath Salts Page 3
- Marijuana

**DISCOUNT:**
30% from 100 grams to 999 grams 50% from 1000 grams and above
All Products in this Category are "Not for Human Consumption" and should be used for chemical research only.

**Top Sellers**

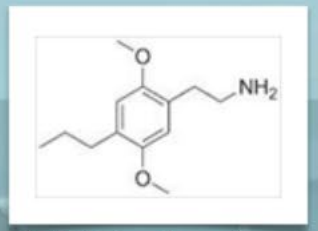
25I-NBOMe
MDPV
Crystal Meth
Methylone
Phenazepam
Pure Bundle
Eight Ballz
iHigh White
Weed
Pulse
C Original
Methiopropamine
Tiger Blood
Crystal Clean
White Lady

**all different amounts ranging from 5gm to 1kg retail and also large amounts at wholesale prices, orders will be sent next day delivery.**
**Shipping from multiple warehouses: China, EU, USA, Russia**



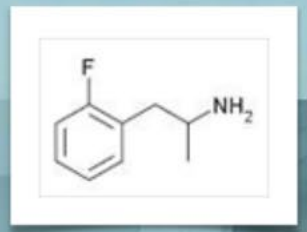
2,5-dimethoxy-4-iodophenethylamine
2C-I (10g) $200
2C-I (100g) $650
2C-I (500) $1800
2C-I (1kg) $2500

Buy Now



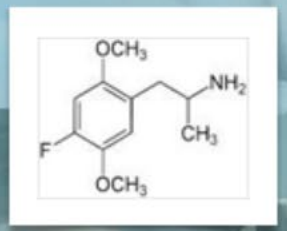
2-(2,5-Dimethoxy-4-propylphenyl)ethanamine
2C-P (10g) $180
2C-P (50g) $350
2C-P (100g) $550
2C-P (1kg) $2500

Buy Now



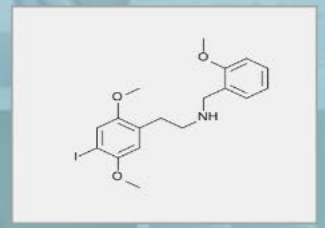
D2Fluromethamphetamine
2-FMA (100g) $450
2-FMA (10g) $150
2-FMA (1kg) $2400
2-FMA (500g) $1200

Buy Now



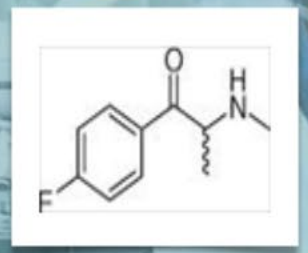
T4-Fluoromethcathinone / Flephedrone
4-FMC (100g) $450
4-FMC (10g) $150
4-FMC (1kg) $2500
4-FMC (500g) $1500

Buy Now



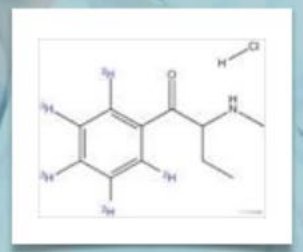
25I-NBOMe
25I-NBOMe
25I-NBOMe (10g) $250
25I-NBOMe(100g) $850
25I-NBOMe(1kg) $4500

Buy Now



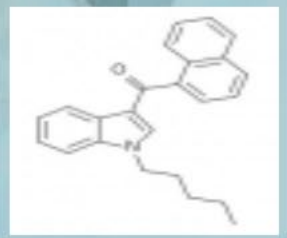
2-(Ethylamino)-1-(4-methylphenyl)propan-1-one
4-MEC (10g) $180
4-MEC (100g) $550
4-MEC (1Kg) $2500
4-MEC (500g) $1400

Buy Now



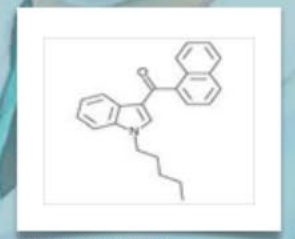
2-(methylamino)-1-phenylbutan-1-one
Buphedrone 10g $200
Buphedrone 100g $550
Buphedrone 1kg $2500
Buphedrone 500g $1500

Buy Now



Naphthalen-1-yl-(1-pentylindol-3-yl) methanone
JWH-018 (10g) $220
JWH-018 (100g) $700
JWH-018 (1kg) $3000
JWH-018 (500g) $1800

Buy Now



naphthalen-1-yl-(1-butylindol-3-yl)methanone
JWH-073 (10g) $150
JWH-073 (100g) $550
JWH-073 (1kg) $2500
JWH-073 (500g) $1300

Buy Now

Crystal Meth (10g) $250
Crystal Meth(100g) $950
Crystal Meth(500g) $2800
Crystal Meth(1kg) $5000

Buy Now

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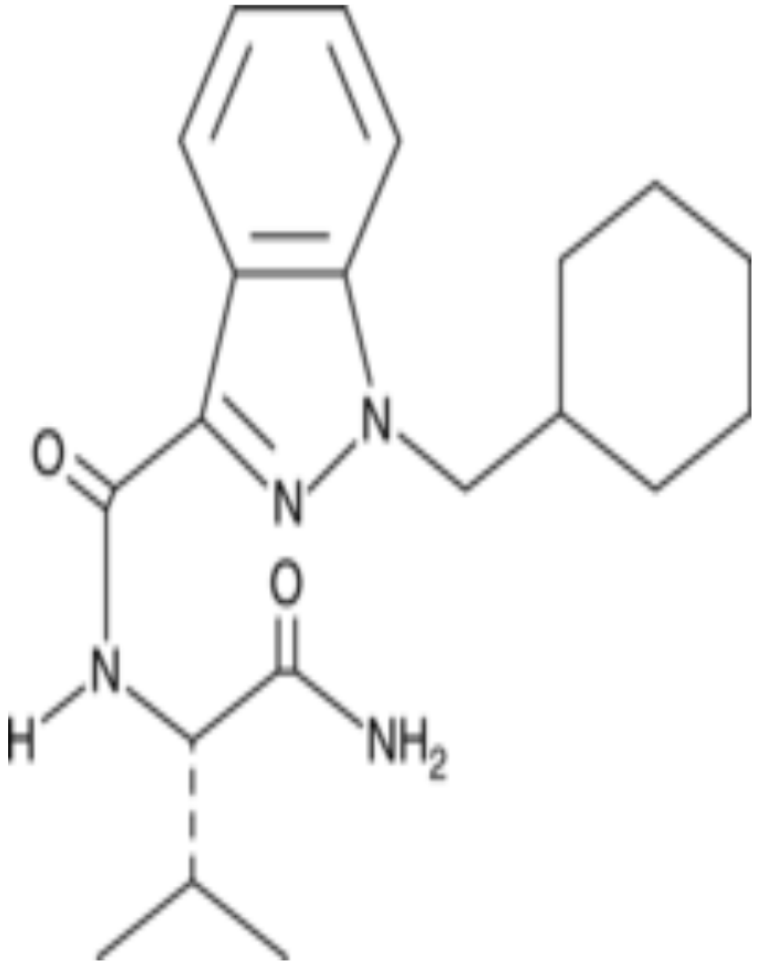


## AB-CHMINACA

$20.00 Per Gram

**Formal Name :** N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide

**CAS Number :** 1185887-21-1

**Molecular Formula :** C20H28N4O2

**Formula Weight :** 356.5

**Formulation :** A crystalline solid

**Purity :** ≥98%

**λmax :** 210, 303 nm

**Stability :** 2 years

1 Add to cart

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# Canadian Connection


# Thank you!




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